

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
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REMARKS

Claims 1, 4 to 9, 11, 18, 27, 38 and 66 to 104 are pending in the present application. Claims 38, 83 to 85, 87, 93 and 98 have been canceled. Claim 88 has been amended herein; new claim 105 has been added herein. Thus, upon entry of the present amendment, claims 1, 4 to 9, 11, 18, 27, 66 to 82, 86, and 88 to 92, 94 to 97, and 99 to 105 will be under examination.

Regarding the amendments

Claim 88 has been amended to recite an oligonucleotide comprising at least 200 contiguous nucleotides. This amendment is supported in the specification, for example, at page 35, lines 13-20. New claim 105 is directed to an oligonucleotide containing a nucleotide sequence consisting of nucleotides 2422-2844 of SEQ ID NO:1 or its complement, or a fragment thereof consisting of at least 30 contiguous nucleotides therefrom, and a nucleotide sequence at the 5' or 3' end that differs from SEQ ID NO:1 or its complement. New claim 105 is supported in the specification, for example, page 15, lines 28-31, which indicates that the LRR domain of NAC corresponds to amino acid residues 808-948 of SEQ ID NO:2 (i.e. nucleotides 2422-2844 of SEQ ID NO:1), and at page 34, lines 7-9.

As set forth above, the amendments and new claim are fully supported by the specification and claims as originally filed and do not introduce new matter. Accordingly, entry of the amendments and new claim is respectfully requested.

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Regarding the sequence listing

The Office Action indicates that sequences disclosed in Figure 1D of the specification are not identified by SEQ ID NOS. In this regard, a Notice to Comply with Requirements for Patent Applications Containing Nucleotide and/or Amino Acid Sequence Disclosures has been issued. Applicant is simultaneously filing a Communication in response to the Notice together with paper and computer readable copies of a substitute sequence listing. The substitute sequence listing is an updated version of the listing submitted May 9, 2000, which has been revised to include each of the amino acid sequence shown in Figure 1D as SEQ ID NOS: 19 to 30. Thus, Applicant requests withdrawal of this objection to the specification.

Regarding the rejection under 35 U.S.C. § 112, first paragraph, enablement

The objection to the specification and corresponding rejection of claims 38, 83 to 85 and 98 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement in the specification, are respectfully traversed.

The Office Action maintains that the specification lacks enabling description of methods for modulating the level of Apaf-1-mediated apoptosis in a cell *in vitro* by expressing NAC in the cell. In particular, the Office Action alleges that Chu et al., J. Biol. Chem. 276:9329-9245 (2001), submitted by Applicant

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as supplementary evidence that NAC and fragments thereof can modulate Apaf-1 mediated apoptosis, describes modulating Apaf-1-mediated apoptosis in the presence of overexpressed Apaf-1 and pro-caspase 9 or overexpressed Apaf-1 and an Apaf-1 apoptosis inducer, and therefore is insufficient evidence that expressing NAC *in vitro* can modulate Apaf-1-mediated apoptosis.

Applicant respectfully maintains that based on the description in the specification of the ability of a polypeptide encoded by SEQ ID NO:2, 4 or 6, or fragment thereof, to bind *in vitro* to apoptosis regulator molecule Apaf-1 (for example, page 76, line 9, to page 81, line 20), and the confirmatory description in Chu et al. of the ability of a NAC polypeptide encoded by SEQ ID NO:2, or a fragment thereof, to bind to Apaf-1 and modulate apoptosis in a cell, those skilled in the art would have been able to use a NAC nucleic acid molecule to modulate Apaf-1-mediated apoptosis as claimed. In particular, one skilled in the art would have routinely sampled a variety of cell types, including those that express pro-caspase 9 and other apoptosis modulators, to confirm the ability of a polypeptide encoded by SEQ ID NO:2, 4 or 6, or fragment thereof, to modulate Apaf-1-mediated apoptosis without undue experimentation.

Nevertheless, claims 38, 83 to 85 and 98 have been canceled herein to further prosecution of the present application. Applicant cancels these claims without prejudice to pursuing them in one or more related applications that claim the benefit of priority to the present application. The enablement rejection is rendered moot in view of the above. Therefore,

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Applicant respectfully requests that the Examiner remove the enablement rejection under 35 U.S.C. § 112, first paragraph.

Regarding the rejection under 35 U.S.C. § 112, second paragraph

The rejection of claims 87 and 88 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, is respectfully traversed.

Claim 87 has been cancelled herein in favor of new claim 105. Thus, the rejection of claim 87 has been rendered moot. New claim 105 is similar to claim 78, which has been indicated to be allowable, but recites an oligonucleotide containing a nucleotide sequence consisting of nucleotides 2422-2844 of SEQ ID NO:1 or its complement, or a fragment thereof consisting of at least 30 contiguous nucleotides therefrom, and a nucleotide sequence at the 5' or 3' end that differs from SEQ ID NO:1 or its complement.

Claim 88 has been amended to recite an oligonucleotide comprising at least 200 contiguous nucleotides of the sequence set forth as nucleotides 3784-3915 of SEQ ID NO:1, or the complement thereof. Antecedent basis for this claim is provided by claim 82, which recites at least 100 contiguous nucleotides of the sequence set forth as nucleotides 3784-3915 of SEQ ID NO:1, or the complement thereof. Therefore, Applicant submits that claim 88 is clear and definite and requests removal of this rejection.

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Regarding the rejections under 35 U.S.C. § 102(a)

The rejection of claims 5, 70 and 75 under 35 U.S.C. § 102(a), as allegedly anticipated by Nagase et al. DNA Res. 6:63-70 (1999) is respectfully traversed. The Office Action alleges that Nagase describes a cDNA clone referenced as KIAA0926 that appears to have >80% identity with SEQ ID NO:1.

Applicant respectfully submits that Nagase et al. does not teach the claimed invention. Specifically, the cDNA clone referenced as KIAA0926 differs from the nucleic acid molecules of claims 5, 70 and 75. Claim 5 is directed to a cDNA containing (depending from claim 1) an isolated nucleic acid molecule containing a nucleotide sequence encoding a polypeptide having at least 80% identity to SEQ ID NO:4 or SEQ ID NO:6, or the complement of the nucleotide sequence, wherein the polypeptide does not contain amino acids 957-987 of SEQ ID NO:2; or (depending from claim 71) an isolated nucleic acid molecule containing a nucleotide sequence encoding a polypeptide having at least 80% identity to SEQ ID NO:2, or the complement of the nucleotide sequence, wherein the polypeptide contains amino acids 1262-1305 of SEQ ID NO:2.

Whereas the nucleic acid molecule of claim 5, depending from claim 1, encodes a polypeptide that does not contain amino acids 957-987 of SEQ ID NO:2, the KIAA0926 polypeptide in fact contains amino acids 957-987 of SEQ ID NO:2. Moreover, whereas the nucleic acid molecule of claim 5, depending from claim 71, encodes a polypeptide containing amino acids 1262-1305 of

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SEQ ID NO:2, the KIAA0926 polypeptide in fact lacks amino acids 1262-1305 of SEQ ID NO:2. This distinction between the amino acid sequences of SEQ ID NO:2 and the KIAA0926 polypeptide is readily apparent from the sequence comparison submitted herewith as Exhibit A. Without teaching the claimed nucleotide sequences, Nagase et al. cannot anticipate claim 5. For these reasons, claim 5 is novel over the cited reference. Applicant therefore requests removal of this rejection under 35 U.S.C. § 102(a).

Claims 70 and 75 are directed to an isolated nucleic acid molecule containing a nucleotide sequence encoding SEQ ID NO:4 or 6 (claim 70); and an isolated nucleic acid molecule containing a nucleotide sequence encoding SEQ ID NO:2 (claim 75). Regarding claim 70, the cited references does not teach SEQ ID NO:4 or 6. With respect to SEQ ID NO:4, the KIAA0926 polypeptide contains a section of amino acid sequence not present in SEQ ID NO:4. As is shown in the amino acid sequence comparison of SEQ ID NO:4 and the KIAA0926 polypeptide submitted as Exhibit B, the KIAA0926 polypeptide contains amino acids 958-987, which are not found in SEQ ID NO:4. With respect to SEQ ID NO:6, the KIAA0926 polypeptide both lacks amino acids 1262-1305 of SEQ ID NO:6 and contains a section of amino acid sequence not present in SEQ ID NO:6 (amino acids 958-987 of KIAA0926). The distinctions between amino acid sequence SEQ ID NO:6 and the KIAA0926 polypeptide is clear from the amino acid comparison submitted as Exhibit C. Thus, Nagase et al. does not teach amino acid sequences SEQ ID NOS:4 or 6, which are recited in claim 70. In view of the above, Applicant submits

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that claim 70 is novel over the cited reference and requests removal of this rejection.

Regarding claim 75, the cited reference does not teach SEQ ID NO:2. As is shown in the amino acid sequence comparison of SEQ ID NO:2 and the KIAA0926 polypeptide submitted herewith as Exhibit A, the KIAA0926 polypeptide lacks amino acids 1262-1305 of SEQ ID NO:2. Without a teaching of amino acid sequence SEQ ID NO:2, the reference cannot anticipate claim 75. In view of the above, Applicant submits that claim 75 is novel over the cited reference and requests removal of this rejection.

The Office Action asserts that post-filing date reference Chu et al. indicates that experiments were performed using a nucleic acid sequence derived from the KIAA0926 cDNA sequence. Applicant respectfully points out that Chu et al. merely states that a BLAST search revealed homology between CARD4/Nod1 and the predicted protein of KIAA0926.

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CONCLUSION

In view of the amendments and the remarks submitted herein, Applicant submits that the claims are in condition for allowance and respectfully requests a notice to that effect. The Examiner is invited to contact the undersigned agent or Cathryn Campbell if there are any questions relating to this application.

Respectfully submitted,

October 20, 2003
Date

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lalign output for KIAA0926 vs. SEQ ID NO:2

[ISREC-Server] Date: Mon Sep 8 20:46:27 MET 2003

LALIGN finds the best local alignments between two sequences version 2.0u66 September 1998 Please cite: X. Huang and W. Miller (1991) Adv. Appl. Math. 12:373-381

Comparison of:

(A) ./wwtmp/lalign/.18931.1.seq KIAA0926

(B) ./wwtmp/lalign/.18931.2.seq SEQ ID NO:2

using matrix file: BL50, gap penalties: -14/-4

97.0% identity in 1473 aa overlap; score: 9515 E(10,000): 0

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      10      20      30      40      50      60
KIAA09 MAGGAWGRLACYLEFLKKEELKEFQLLLANKAHSRSSSGETPAQPEKTSGMEVASYLVAQ
      .....
SEQ    MAGGAWGRLACYLEFLKKEELKEFQLLLANKAHSRSSSGETPAQPEKTSGMEVASYLVAQ
      10      20      30      40      50      60

      70      80      90     100     110     120
KIAA09 YGEQRAWDLALHTWEQMGLRSLCAQAQEGAGHSPSPFPYSPSEPHLGSPSQPTSTAVLMPW
      .....
SEQ    YGEQRAWDLALHTWEQMGLRSLCAQAQEGAGHSPSPFPYSPSEPHLGSPSQPTSTAVLMPW
      70      80      90     100     110     120

      130     140     150     160     170     180
KIAA09 IHLPAGCTQGSERRVLRQLPDTSGRRWREISASLLYQALPSSPDHESPSQESPNAPTST
      .....
SEQ    IHLPAGCTQGSERRVLRQLPDTSGRRWREISASLLYQALPSSPDHESPSQESPNAPTST
      130     140     150     160     170     180

      190     200     210     220     230     240
KIAA09 AVLGSWGSPQPQSLAPREQEAPGTQWPLDETSGIYYTEIREREREKSEKGRPPWAAVVG
      .....
SEQ    AVLGSWGSPQPQSLAPREQEAPGTQWPLDETSGIYYTEIREREREKSEKGRPPWAAVVG
      190     200     210     220     230     240

      250     260     270     280     290     300
KIAA09 PPQAHTSLQPHHPWEPVRESLCSTWPWKNEFDNQKFTQLLLLQRPHPRSQDPLVKRSW
      .....
SEQ    PPQAHTSLQPHHPWEPVRESLCSTWPWKNEFDNQKFTQLLLLQRPHPRSQDPLVKRSW
      250     260     270     280     290     300

      310     320     330     340     350     360
KIAA09 PDYVEENRGHLIEIRDLFGPGLDTQEPRIVILQGAAGIGKSTLARQVKEAWGRGQLYGDR
      .....
SEQ    PDYVEENRGHLIEIRDLFGPGLDTQEPRIVILQGAAGIGKSTLARQVKEAWGRGQLYGDR
      310     320     330     340     350     360

      370     380     390     400     410     420
KIAA09 FQHVIFYFSCRELAQSKVVS LAELIGKDG TATPAPIRQILSRPERLLFILDGVDEPGWVLQ
      .....

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EXHIBIT A

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SEQ      FQHVIFYFSCRELAQSKVVSLAELIGKDGATPAPIRQILSRPERLLFILDGVDEPGWVLQ
          370      380      390      400      410      420
          430      440      450      460      470      480
KIAA09  EPSSELCLHWSQPQPADALLGSLGKTLPEASFLITARTTALQNLIPSLEQARWVEVLG
          .....
SEQ      EPSSELCLHWSQPQPADALLGSLGKTLPEASFLITARTTALQNLIPSLEQARWVEVLG
          430      440      450      460      470      480
          490      500      510      520      530      540
KIAA09  FSESSRKEYFYRYFTDERQAIRAFRLVKSNNKELWALCLVPVSWLACTCLMQMKRKEKL
          .....
SEQ      FSESSRKEYFYRYFTDERQAIRAFRLVKSNNKELWALCLVPVSWLACTCLMQMKRKEKL
          490      500      510      520      530      540
          550      560      570      580      590      600
KIAA09  TLTSKTTTTLCLHYLAQALQAQPLGQRLDLCSLAAGIWQKKTFLSPDDLRLKHGLDGAI
          .....
SEQ      TLTSKTTTTLCLHYLAQALQAQPLGQRLDLCSLAAGIWQKKTFLSPDDLRLKHGLDGAI
          550      560      570      580      590      600
          610      620      630      640      650      660
KIAA09  ISTFLKMGILQEHPISYSFIHLCFQEFAAMSYVLEDEKGRGKHSNCIIDLEKTLEAY
          .....
SEQ      ISTFLKMGILQEHPISYSFIHLCFQEFAAMSYVLEDEKGRGKHSNCIIDLEKTLEAY
          610      620      630      640      650      660
          670      680      690      700      710      720
KIAA09  GIHGLFGASTTRFLLGLLSDEGEREMENIFHCRLSQGRNLMQWVPSLQLLLQPHSLES LH
          .....
SEQ      GIHGLFGASTTRFLLGLLSDEGEREMENIFHCRLSQGRNLMQWVPSLQLLLQPHSLES LH
          670      680      690      700      710      720
          730      740      750      760      770      780
KIAA09  CLYETRNTKFTLTQVMAHFEEMGMCVETDMELLVCTFCIKFSRHVKKLQLIEGRQHRSTWS
          .....
SEQ      CLYETRNTKFTLTQVMAHFEEMGMCVETDMELLVCTFCIKFSRHVKKLQLIEGRQHRSTWS
          730      740      750      760      770      780
          790      800      810      820      830      840
KIAA09  PTMVVLFWRVPVTDAYWQILFSVLKVTRNLKELDLSGNSLSHSAVKS LCKTLRRPCLLE
          .....
SEQ      PTMVVLFWRVPVTDAYWQILFSVLKVTRNLKELDLSGNSLSHSAVKS LCKTLRRPCLLE
          790      800      810      820      830      840
          850      860      870      880      890      900
KIAA09  TLRLAGCGLTAEDCKDLAFGLRANQTLTELDLSFNVLTDAGAKHLCQRLRQPSCKLQRLQ
          .....
SEQ      TLRLAGCGLTAEDCKDLAFGLRANQTLTELDLSFNVLTDAGAKHLCQRLRQPSCKLQRLQ
          850      860      870      880      890      900
          910      920      930      940      950      960
KIAA09  LVSCGLTSDCCQDLASVLSASPSLKELDLQQNNLDDVGVRLLCEGLRHPPACKLIRLGLDQ
          .....
SEQ      LVSCGLTSDCCQDLASVLSASPSLKELDLQQNNLDDVGVRLLCEGLRHPPACKLIRLGLDQ
          910      920      930      940      950      960
          970      980      990      1000      1010      1020
KIAA09  TTLSDEMQRQELRALEQEKPLLIFSRRKPSVMTPTGLDTGEMSNSTSSSLKRQRLGSERA
          .....
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SEQ      TTLSDEMRQELRALEQEKPELLIFSRRKPSVMTPTTEGLDTGEMSNSTSSLKRQRLGSERA
          970          980          990          1000          1010          1020

          1030          1040          1050          1060          1070          1080
KIAA09  ASHVAQANLKLLDVSKIFPIAEIAEESSPEVVPVELLCVPSPASQGDHLTKPLGTDDDFW
          .....
SEQ      ASHVAQANLKLLDVSKIFPIAEIAEESSPEVVPVELLCVPSPASQGDHLTKPLGTDDDFW
          1030          1040          1050          1060          1070          1080

          1090          1100          1110          1120          1130          1140
KIAA09  GPTGPGVATEVVDKEKNLYRVHFPVAGSYRWPNTGLCFVMREAVTVEIEFCVWDQFLGEIN
          .....
SEQ      GPTGPGVATEVVDKEKNLYRVHFPVAGSYRWPNTGLCFVMREAVTVEIEFCVWDQFLGEIN
          1090          1100          1110          1120          1130          1140

          1150          1160          1170          1180          1190          1200
KIAA09  PQHSHWMVAGPLLDIKAEPGAVEAVHLPHFVALQGGHVDTSLFQMAHFKEEGMLLEKPARV
          .....
SEQ      PQHSHWMVAGPLLDIKAEPGAVEAVHLPHFVALQGGHVDTSLFQMAHFKEEGMLLEKPARV
          1150          1160          1170          1180          1190          1200

          1210          1220          1230          1240          1250          1260
KIAA09  ELHHIVLENPSFSPLGVLLKMIHNALRFIPVTSVLLYHRVHPPEVTFHLYLIPSDCSIR
          .....
SEQ      ELHHIVLENPSFSPLGVLLKMIHNALRFIPVTSVLLYHRVHPPEVTFHLYLIPSDCSIR
          1210          1220          1230          1240          1250          1260

                                     1270
KIAA09  K-----ELELCYRSPGEDQLF
          :
          .....
SEQ      KAIDDLKMFQFVRIHKPPPLTPLYMGCRTVSGSGSGLMELPKLELCYRSPGEDQLF
          1270          1280          1290          1300          1310          1320

          1280          1290          1300          1310          1320          1330
KIAA09  SEFYVGHGSGIRLQVKDKKDETLVWEALVKPGDLMPATTLIPPARIAVPSPLDAPQLLH
          .....
SEQ      SEFYVGHGSGIRLQVKDKKDETLVWEALVKPGDLMPATTLIPPARIAVPSPLDAPQLLH
          1330          1340          1350          1360          1370          1380

          1340          1350          1360          1370          1380          1390
KIAA09  FVDQYREQLIARVTSVEVVLDKLHGQVLSQEYERVLAENTRPSQMRKLFSLSQSWDRKC
          .....
SEQ      FVDQYREQLIARVTSVEVVLDKLHGQVLSQEYERVLAENTRPSQMRKLFSLSQSWDRKC
          1390          1400          1410          1420          1430          1440

          1400          1410          1420
KIAA09  KDGLYQALKETHPHLIMELWEKGSKKGLLPLSS
          .....
SEQ      KDGLYQALKETHPHLIMELWEKGSKKGLLPLSS
          1450          1460          1470

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44.6% identity in 121 aa overlap; score: 336 E(10,000): 1.2e-21

```

          870          880          890          900          910          920
KIAA09  LRANQTLTELDLSFNVLTDAGAKHLCQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSA
          .....
SEQ      LKVTRNLKELDLGNSLSHSAVKSCKTLRRPRCLLETLRLAGCGLTAEDCKDLAFGLRA
          810          820          830          840          850          860

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          930          940          950          960          970          980
KIAA09 SPSLKELDLQQNNLDDVGVRLLCEGLRHPACKLIRLGLDQTTLSDEMRQELRALEQEKPO
      . . . : : : : : : : : : : : : : : : : : : : : : : : :
SEQ    NQTLTELDLSFNVLTDAKAKHLCQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSASPS
          870          880          890          900          910          920

```

```

KIAA09 L
:
SEQ    L

```

44.6% identity in 121 aa overlap; score: 336 E(10,000): 1.2e-21

```

          810          820          830          840          850          860
KIAA09 LKVTRNLKELDLSGNSLSHSAVKSLCKTLRRPRCLLETLRLAGCGLTAEDCKDLAFGLRA
      : : : : : : : : : : : : : : : : : : : : : : : :
SEQ    LRANQTLTELDLSFNVLTDAKAKHLCQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSA
          870          880          890          900          910          920

```

```

          870          880          890          900          910          920
KIAA09 NQTLTELDLSFNVLTDAKAKHLCQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSASPS
      . . . : : : : : : : : : : : : : : : : : : : : :
SEQ    SPSLKELDLQQNNLDDVGVRLLCEGLRHPACKLIRLGLDQTTLSDEMRQELRALEQEKPO
          930          940          950          960          970          980

```

```

KIAA09 L
:
SEQ    L

```

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lalign output for KIAA0926 vs. SEQ ID NO:4

[ISREC-Server] Date: Mon Sep 8 20:45:18 MET 2003

LALIGN finds the best local alignments between two sequences version 2.0u66 September 1998 Please cite: X. Huang and W. Miller (1991) Adv. Appl. Math. 12:373-381

Comparison of:

(A) ./wwtmp/lalign/.22593.1.seq KIAA0926

(B) ./wwtmp/lalign/.22593.2.seq SEQ ID NO:4

using matrix file: BL50, gap penalties: -14/-4

97.9% identity in 1429 aa overlap; score: 9384 E(10,000): 0

```

      10      20      30      40      50      60
KIAA09 MAGGAWGRLACYLEFLKKEELKEFQLLLANKAHSRSSSGETPAQPEKTSGMELVASYLVAQ
      .....
SEQ     MAGGAWGRLACYLEFLKKEELKEFQLLLANKAHSRSSSGETPAQPEKTSGMELVASYLVAQ
      10      20      30      40      50      60

      70      80      90     100     110     120
KIAA09 YGEQRAWDLALHTWEQMGLRSLCAQAQEGAGHSPSPFPYSPSEPHLGSPSQPTSTAVLMPW
      .....
SEQ     YGEQRAWDLALHTWEQMGLRSLCAQAQEGAGHSPSPFPYSPSEPHLGSPSQPTSTAVLMPW
      70      80      90     100     110     120

      130     140     150     160     170     180
KIAA09 IHHELPAGCTQGSERRVLRQLPDTSGRRWREISASLLYQALPSSPDHESPSQESPNAPTST
      .....
SEQ     IHHELPAGCTQGSERRVLRQLPDTSGRRWREISASLLYQALPSSPDHESPSQESPNAPTST
      130     140     150     160     170     180

      190     200     210     220     230     240
KIAA09 AVLGSWGSPQPQSLAPREQEAPGTQWPLDETSGIYYTEIREREREKSEKGRPPWAAVVG
      .....
SEQ     AVLGSWGSPQPQSLAPREQEAPGTQWPLDETSGIYYTEIREREREKSEKGRPPWAAVVG
      190     200     210     220     230     240

      250     260     270     280     290     300
KIAA09 PPQAHTSLQPHHPWEPSVRESLCSTWPWKNEFDNQFTQLLLLQRPHPRSQDPLVKRSW
      .....
SEQ     PPQAHTSLQPHHPWEPSVRESLCSTWPWKNEFDNQFTQLLLLQRPHPRSQDPLVKRSW
      250     260     270     280     290     300

      310     320     330     340     350     360
KIAA09 PDYVEENRGHLIEIRDLFGPGLDTQEPRIVILQGAAGIGKSTLARQVKEAWGRGQLYGDR
      .....
SEQ     PDYVEENRGHLIEIRDLFGPGLDTQEPRIVILQGAAGIGKSTLARQVKEAWGRGQLYGDR
      310     320     330     340     350     360

      370     380     390     400     410     420
KIAA09 FQHVVFYFSCRELAQSKVVSLELIGKDGATATPAPIRQILSRPERLLFILDGVDEPGWVLQ
      .....

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EXHIBIT B

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SEQ      FQHVFYFSCRELAQSKVVSLAELIGKDGTTATPAPIRQILSRPERLLFILDGVDEPGWVLQ
          370      380      390      400      410      420

          430      440      450      460      470      480
KIAA09  EPSSELCLHWSQPQPADALLGSLGKTILPEASFLITARTTALQNLIPSLEQARWVEVLG
          .....
SEQ      EPSSELCLHWSQPQPADALLGSLGKTILPEASFLITARTTALQNLIPSLEQARWVEVLG
          430      440      450      460      470      480

          490      500      510      520      530      540
KIAA09  FSESSRKEYFYRYFTDERQAIRAFRLVKSNEKELWALCLVPVWSWLACTCLMQQMKRKEKL
          .....
SEQ      FSESSRKEYFYRYFTDERQAIRAFRLVKSNEKELWALCLVPVWSWLACTCLMQQMKRKEKL
          490      500      510      520      530      540

          550      560      570      580      590      600
KIAA09  TLTSKTTTTLCLHYLAQALQAQPLGPQLRDLCSLAAEGIWQKKTFLSPDDLRLKHGLDGAI
          .....
SEQ      TLTSKTTTTLCLHYLAQALQAQPLGPQLRDLCSLAAEGIWQKKTFLSPDDLRLKHGLDGAI
          550      560      570      580      590      600

          610      620      630      640      650      660
KIAA09  ISTFLKMGILQEHPILSYSFIHLCFQEFAAMSYLEDEKGRGKHSNCIIDLEKTLEAY
          .....
SEQ      ISTFLKMGILQEHPILSYSFIHLCFQEFAAMSYLEDEKGRGKHSNCIIDLEKTLEAY
          610      620      630      640      650      660

          670      680      690      700      710      720
KIAA09  GIHGLFGASTTRFLLGLLSDEGEREMENIFHCRLSQGRNLMQWVPSLQLLLQPHSLESLSH
          .....
SEQ      GIHGLFGASTTRFLLGLLSDEGEREMENIFHCRLSQGRNLMQWVPSLQLLLQPHSLESLSH
          670      680      690      700      710      720

          730      740      750      760      770      780
KIAA09  CLYETRNTKFTLTQVMAHFEEMGMCVETDMELLVCTFCIKFSRHVKKLQLIEGRQHRSTWS
          .....
SEQ      CLYETRNTKFTLTQVMAHFEEMGMCVETDMELLVCTFCIKFSRHVKKLQLIEGRQHRSTWS
          730      740      750      760      770      780

          790      800      810      820      830      840
KIAA09  PTMVVLFWRVPVTDAYWQILFSVLKVTRNLKELDLSGNSLSHSAVKSICKTLRRPRLLE
          .....
SEQ      PTMVVLFWRVPVTDAYWQILFSVLKVTRNLKELDLSGNSLSHSAVKSICKTLRRPRLLE
          790      800      810      820      830      840

          850      860      870      880      890      900
KIAA09  TLRLAGCGLTAEDCKDLAFGLRANQTLTELDLSFNVLTADAGAKHLCQRLRQPSCKLQRLQ
          .....
SEQ      TLRLAGCGLTAEDCKDLAFGLRANQTLTELDLSFNVLTADAGAKHLCQRLRQPSCKLQRLQ
          850      860      870      880      890      900

          910      920      930      940      950      960
KIAA09  LVSCGLTSDCCQDLASVLSASPSLKELDLQNNLDDVGVRLLCGLRHPACKLIRLGLDQ
          .....
SEQ      LVSCGLTSDCCQDLASVLSASPSLKELDLQNNLDDVGVRLLCGLRHPACKLIRLG---
          910      920      930      940      950

          970      980      990      1000      1010      1020
KIAA09  TTLSDEMROELRALEQEKPOLLIFFSRRKPSVMTPTGLDTGEMSNSTSSSLKRQRLGSERA
          .....

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SEQ      -----KPSVMTPTTEGLDTGEMSNSTSSSLKRQRLGSERA
              960      970      980      990

      1030      1040      1050      1060      1070      1080
KIAA09 ASHVAQANLKLLDVS KIFPIAEIAEESSPEVVPVELLCVPSPASQGD LHTKPLGTDDDFW
      .....
SEQ     ASHVAQANLKLLDVS KIFPIAEIAEESSPEVVPVELLCVPSPASQGD LHTKPLGTDDDFW
      1000      1010      1020      1030      1040      1050

      1090      1100      1110      1120      1130      1140
KIAA09 GPTGPVATEVVDKEKNLYRVHFPVAGSYRWPNTGLCFVMREAVTVEIEFCVWDQFLGEIN
      .....
SEQ     GPTGPVATEVVDKEKNLYRVHFPVAGSYRWPNTGLCFVMREAVTVEIEFCVWDQFLGEIN
      1060      1070      1080      1090      1100      1110

      1150      1160      1170      1180      1190      1200
KIAA09 PQHSWMVAGPLLDIKAEPGAVEAVHLPHPFVALQGGHVDTS LFM AHFKKEEGMLLEKPARV
      .....
SEQ     PQHSWMVAGPLLDIKAEPGAVEAVHLPHPFVALQGGHVDTS LFM AHFKKEEGMLLEKPARV
      1120      1130      1140      1150      1160      1170

      1210      1220      1230      1240      1250      1260
KIAA09 ELHHIVLENPSFSPLGVLLKMIHNALRFIPVTSV VLLYHRVHP EEVTFHLYLIPSDCSIR
      .....
SEQ     ELHHIVLENPSFSPLGVLLKMIHNALRFIPVTSV VLLYHRVHP EEVTFHLYLIPSDCSIR
      1180      1190      1200      1210      1220      1230

      1270      1280      1290      1300      1310      1320
KIAA09 KELELCYRSPGEDQLFSEFYVGH LGSGIRLQVKDKKDETLVWEALVKPGDLMPATTLIPP
      .....
SEQ     KELELCYRSPGEDQLFSEFYVGH LGSGIRLQVKDKKDETLVWEALVKPGDLMPATTLIPP
      1240      1250      1260      1270      1280      1290

      1330      1340      1350      1360      1370      1380
KIAA09 ARIAVPSPLDAPQLLHFVDQYREQLIARVTSVEVVLDK LHGQVLSQE QYERVLAENTRPS
      .....
SEQ     ARIAVPSPLDAPQLLHFVDQYREQLIARVTSVEVVLDK LHGQVLSQE QYERVLAENTRPS
      1300      1310      1320      1330      1340      1350

      1390      1400      1410      1420
KIAA09 QMRKLFSLSQSWDRKCKDGLYQALKETHPHLIMELWEKGSKKGLLPLSS
      .....
SEQ     QMRKLFSLSQSWDRKCKDGLYQALKETHPHLIMELWEKGSKKGLLPLSS
      1360      1370      1380      1390

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44.6% identity in 121 aa overlap; score: 336 E(10,000): 1.1e-21

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      870      880      890      900      910      920
KIAA09 LRANQTLTELDLSFNVLT DAKAHL CQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSA
      .....
SEQ     LKVTRNLKELDLSGNSLSHSAVKS LCKTLRRPRCLLET LRLAGCGLTAEDCKDLAFLRA
      810      820      830      840      850      860

      930      940      950      960      970      980
KIAA09 SPSLKELDLQNNLDDVGVRLLCEGLRHPACKLIRLGLDQT TSLDEM RQELRALEQEK PQ
      .....
SEQ     NQTLTELDLSFNVLT DAKAHL CQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSASPS
      870      880      890      900      910      920

```

KIAA09 L

:
SEQ L

43.7% identity in 126 aa overlap; score: 316 E(10,000): 6.7e-20

	810	820	830	840	850	860
KIAA09	LKVTRNLKELDL	SGNSLSHSAVKS	LCKTLRRPRCL	LETLRLAGCGL	TAEDCKDLA	FLGLRA
SEQ	LRANQTLTELD	LSFNVLTDA	GAHLCQRLR	QPSCKLQRL	QLVSCGLT	SDCCQDLASVLSA
	870	880	890	900	910	920

	870	880	890	900	910	920
KIAA09	NQTLTELDLS	FNVLTDAGAK	HLCQRLRQ	PSCKLQRL	QLVSCGLT	SDCCQDLASVLSASPS
SEQ	SPSLKELDL	QQNNLDDV	GVRLLC	EGLRHPACK	LIRLGKPSV	-MTPTEGLDTGEMSNSTSS
	930	940	950	960	970	

KIAA09 LKELDL

:
SEQ LKRQRL
980

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lalign output for KIAA0926 vs. SEQ ID NO:6

[ISREC-Server] Date: Mon Sep 8 20:44:06 MET 2003

LALIGN finds the best local alignments between two sequences version 2.0u66 September 1998 Please cite: X. Huang and W. Miller (1991) Adv. Appl. Math. 12:373-381

Comparison of:

(A) ./wwtmp/lalign/.16138.1.seq KIAA0926

(B) ./wwtmp/lalign/.16138.2.seq SEQ ID NO:6

using matrix file: BL50, gap penalties: -14/-4

95.0% identity in 1473 aa overlap; score: 9198 E(10,000): 0

```

      10      20      30      40      50      60
KIAA09 MAGGAWGRLACYLEFLKKEELKEFQLLLANKAHSRSSSGETPAQPEKTS GMEVASYLVAQ
      .....
SEQ     MAGGAWGRLACYLEFLKKEELKEFQLLLANKAHSRSSSGETPAQPEKTS GMEVASYLVAQ
      10      20      30      40      50      60

      70      80      90     100     110     120
KIAA09 YGEQRAWDLALHTWQMGLRSLCAQAQEGAGHSPSPFPYSPSEPHLGSPSQPTSTAVLMPW
      .....
SEQ     YGEQRAWDLALHTWQMGLRSLCAQAQEGAGHSPSPFPYSPSEPHLGSPSQPTSTAVLMPW
      70      80      90     100     110     120

      130     140     150     160     170     180
KIAA09 IHELPAGCTQGSERRVLRQLPDTSGRRWREISASLLYQALPSSPDHESPSQESPNAPTST
      .....
SEQ     IHELPAGCTQGSERRVLRQLPDTSGRRWREISASLLYQALPSSPDHESPSQESPNAPTST
      130     140     150     160     170     180

      190     200     210     220     230     240
KIAA09 AVLGSWGSPQPQSLAPREQEAPGTQWPLDETSGIYYTEIREREREKSEKGRPPWAAVVG
      .....
SEQ     AVLGSWGSPQPQSLAPREQEAPGTQWPLDETSGIYYTEIREREREKSEKGRPPWAAVVG
      190     200     210     220     230     240

      250     260     270     280     290     300
KIAA09 PPQAHTSLQPHHPWEPVRESLCSTWPWKNEFDNQKFTQLLLLQRP HPRSQDPLVKRSW
      .....
SEQ     PPQAHTSLQPHHPWEPVRESLCSTWPWKNEFDNQKFTQLLLLQRP HPRSQDPLVKRSW
      250     260     270     280     290     300

      310     320     330     340     350     360
KIAA09 PDYVEENRGHLIEIRDLFGPGLDTQEPRIVILQGAAGIGKSTLARQVKEAWGRGQLYGDR
      .....
SEQ     PDYVEENRGHLIEIRDLFGPGLDTQEPRIVILQGAAGIGKSTLARQVKEAWGRGQLYGDR
      310     320     330     340     350     360

      370     380     390     400     410     420
KIAA09 FQHVFYFSCRELAQSKVVS LAELIGKDG TATPAPIRQILSRPERLLFILDGVDEPGWVLQ
      .....

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EXHIBIT C

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SEQ      FQHVFYFSCRELAQSKVVS LAELIGKDG TATPAPIRQILSRPERLLFILDGVDEPGWVLQ
          370      380      390      400      410      420

          430      440      450      460      470      480
KIAA09 EPSSSELCLHWSQPQPADALLGSL LGKTI LPEASFLITARTTALQNLIPSLEQARWVEVLG
          .....
SEQ      EPSSSELCLHWSQPQPADALLGSL LGKTI LPEASFLITARTTALQNLIPSLEQARWVEVLG
          430      440      450      460      470      480

          490      500      510      520      530      540
KIAA09 FSESSRKEYFYRYFTDERQAIRAFRLVKS NKELWALCLVPVSWLACTCLMQMKRKEKL
          .....
SEQ      FSESSRKEYFYRYFTDERQAIRAFRLVKS NKELWALCLVPVSWLACTCLMQMKRKEKL
          490      500      510      520      530      540

          550      560      570      580      590      600
KIAA09 TLTSKTTTTLCLHYLAQALQAQPLGPQLRDLCSLA AEGIWQKKTLFSPDDL RKHGLDGAI
          .....
SEQ      TLTSKTTTTLCLHYLAQALQAQPLGPQLRDLCSLA AEGIWQKKTLFSPDDL RKHGLDGAI
          550      560      570      580      590      600

          610      620      630      640      650      660
KIAA09 ISTFLKMGILQEHP IPLSYF IHLCFQE FFAAMSYVLEDEKGRGKHSNCI IDLEKTLEAY
          .....
SEQ      ISTFLKMGILQEHP IPLSYF IHLCFQE FFAAMSYVLEDEKGRGKHSNCI IDLEKTLEAY
          610      620      630      640      650      660

          670      680      690      700      710      720
KIAA09 GIHGLFGASTTRFLLG LLSDEGEREMENIFHCRLS QGRNLMQWVPSLQ LLLQPHSLES LH
          .....
SEQ      GIHGLFGASTTRFLLG LLSDEGEREMENIFHCRLS QGRNLMQWVPSLQ LLLQPHSLES LH
          670      680      690      700      710      720

          730      740      750      760      770      780
KIAA09 CLYETR NKTF LTQVMAHFEEMGMCVETDMELLVCTFCIKFSRHVKKLQ LIEGRQHRSTWS
          .....
SEQ      CLYETR NKTF LTQVMAHFEEMGMCVETDMELLVCTFCIKFSRHVKKLQ LIEGRQHRSTWS
          730      740      750      760      770      780

          790      800      810      820      830      840
KIAA09 PTMVV LFRWVPVTDAYWQILF SVLKVTRNLKELDL SGNLSL SHSAVKS LCKTLRRPRCLLE
          .....
SEQ      PTMVV LFRWVPVTDAYWQILF SVLKVTRNLKELDL SGNLSL SHSAVKS LCKTLRRPRCLLE
          790      800      810      820      830      840

          850      860      870      880      890      900
KIAA09 TLRLAGCGLTAEDCKDLAFGLRANQTL TELDLSF NVLTDAGAKHLCQRLRQPSCKLQRLQ
          .....
SEQ      TLRLAGCGLTAEDCKDLAFGLRANQTL TELDLSF NVLTDAGAKHLCQRLRQPSCKLQRLQ
          850      860      870      880      890      900

          910      920      930      940      950      960
KIAA09 LVSCGLTSDCCQDLASVLSASPSL KELD LQQNNLDDVGVRLLCEGLRHPACKLIRLGLDQ
          .....
SEQ      LVSCGLTSDCCQDLASVLSASPSL KELD LQQNNLDDVGVRLLCEGLRHPACKLIRLG---
          910      920      930      940      950

          970      980      990      1000      1010      1020
KIAA09 TTLSDEM RQELRALEQEK PQLLI FSRRKPSVMTPT EGLDTGEMSNSTSSLKRQRLG SERA
          .....

```

44.6% identity in 121 aa overlap; score: 336 E(10,000): 1.2e-21

9/8/2003

```

          930          940          950          960          970          980
KIAA09 SPSLKELDLQQNNLDDVGVRLLCEGLRHPACKLIRLGLDQTTLSDEMRQELRALEQEKPQ
      . . . : : : : : : : : : : : : : : : : : : : : : : : : : :
SEQ    NQTLTELDLSFNVLTDAKHLHCQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSASPS
          870          880          890          900          910          920

```

KIAA09 L

:

SEQ L

43.7% identity in 126 aa overlap; score: 316 E(10,000): 7e-20

```

          810          820          830          840          850          860
KIAA09 LKVTRNLKELDLSGNSLSHSAVKSLCKTLRRPRCLLETLRLAGCGLTAEDCKDLAFGLRA
      : : : : : : : : : : : : : : : : : : : : : : : : : :
SEQ    LRANQTLTELDLSFNVLTDAKHLHCQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSA
          870          880          890          900          910          920

```

```

          870          880          890          900          910          920
KIAA09 NQTLTELDLSFNVLTDAKHLHCQRLRQPSCKLQRLQLVSCGLTSDCCQDLASVLSASPS
      . . . : : : : : : : : : : : : : : : : : : : : :
SEQ    SPSLKELDLQQNNLDDVGVRLLCEGLRHPACKLIRLKGPSV-MTPTEGLDTGEMSNSTSS
          930          940          950          960          970

```

KIAA09 LKELDL

: : :

SEQ LKRQRL
980

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